REMARKS

Claims 68-81 are pending in the subject application with claims 82-106 withdrawn from consideration. Applicants have hereinabove amended claim 68. In addition applicants have cancelled claims 75-76, and claims 82-106 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in the future.

Support for the amendments to claims 68 can be found *inter alia* in the specification as originally filed at page 13, lines 24-26; page 16, lines 11-13; page 26, lines 13-16 and figure 4B. Accordingly, applicants maintain that amended claim 68 introduces no new matter and is fully supported by the application as originally filed.

Rejection Under 35 U.S.C. 102(b)- Novelty

The Examiner rejected claims 68-81 under 35 U.S.C. 102(b) as being anticipated by Simmons *et al.* (1994, Advances in Bone Marrow Purging and Processing: Fourth Symposium 389, pages 271-280). The Examiner asserted that Simmons *et al.* teach an enriched cell population of mesenchymal precursor cells that are capable of giving rise to CFU-F and a composition comprising said cells. The Examiner also asserted that Simmons *et al.* teach that said enriched cell population carries the antigen identified by STRO-1 antibody and that said cells are also positive for VCAM, LFA-3, THY-1, P-selectin, L-selectin, CD49b/CD29 surface markers (see Table 1 in particular). The Examiner further asserted that Simmons *et al.*, teach that said cells are capable of differentiation into at least adipocytes, osteoblasts and

fibroblast. The Examiner acknowledged that the reference is silent about said enriched cell population of mesenchymal precursors being positive for cell markers 3G5 or MUC18/cd146, as recited in claims 71-76, or positive for one or more markers recited in claim 77, or negative for the markers recited in claim 78, or capable of forming a clonogenic colony as recited in claims 80 and 81. The Examiner asserted, however, that these limitations would be inherent properties of the referenced cell composition because the referenced cell composition is allegedly the same as claimed. The Examiner asserted that it is applicants' burden to show that the referenced cell population does not have the same properties as recited in the claims.

The Examiner also asserted that the arguments of counsel cannot take the place of evidence in the record.

The Examiner also rejected claims 70 and 79 asserting that the claimed functional limitation would be an inherent property of the referenced enriched cell population and composition comprising said cells.

Applicants' Response

In response, applicants respectively traverse the Examiner's rejection. However, in order to expedite the prosecution of the subject application, applicants have hereinabove amended claim 68.

With regard to Examiner's assertion that the arguments of counsel cannot take place of evidence in the record, the

applicants respectfully note that (1) evidence in the specification is evidence of record and (2) further evidence is not required in the present case because the novelty of the claimed invention is clear on the face of the evidence provided in the specification.

Applicants submit that amended claim 68 recites "A population of cells enriched for 3G5 cells, wherein such 3G5 cells are mesenchymal precursor cells which comprise mesenchymal precursor cells capable of giving rise to colony forming unit-fibroblast (CFU-F), and wherein at least 30% of the total cells of the population are positive for the marker 3G5" (emphasis added).

Simmons *et al.* describe enrichment of a population of cells with STRO-1^{+} MPCs but not wherein at least 30% of the total cells are positive for the marker 3G5.

As explained in the specification on page 13, lines 24 to 26, "3G5 positive MPCs constitute about 15% of MPCs based on STRO-1^{bri} colony forming cells" (emphasis added). Accordingly, isolation of MPCs from bone marrow based on enrichment of cells expressing the STRO-1 marker by Simmons et al. cannot result in a population enriched for 3G5+ cells wherein at least 30% of the total cells are positive for the marker 3G5.

The Examiner has acknowledged that the reference is silent about cell marker MUC18/cdl46 as recited in claims 71-74, or that the population is positive for one or more markers recited in claim 77, or negative for the markers recited in

claim 78, or capable of forming a clonogenic colony as recited in claims 80 and 81. These limitations would not be inherent properties (to the extent an anticipation rejection based on inherency requires certainty) of the referenced cell composition because the referenced cell composition is not the same as the claimed invention as explained above. Therefore, applicants submit that Simmons *et al.* do not anticipate the claimed invention.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Under 35 U.S.C. 102(e) - Novelty

The Examiner rejected claims 68-81 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 7,122,178 (issued to Simmons *et al.*, 2006) or U.S. Patent Application No. 2005/0281790 or WO 01/04268.

The Examiner asserted that U.S. Patent No. 7,122,178 teaches an enriched cell population of mesenchymal precursor cells, wherein said composition are enriched for STRO-1^{bright} cells and wherein said cells are capable of giving rise to CFU-F (see entire document, claims 1-13 in particular).

The Examiner also asserted that U.S. Patent Application No. 2005/0281790 teaches an enriched cell population of mesenchymal precursor cells, wherein said composition are enriched for STRO-1^{bright} cells and wherein said cells are

capable of giving rise to CFU-F (see entire document, claims 52-78 in particular).

The Examiner acknowledged that the references (i.e. U.S. Patent No. 7,122,178, and U.S. Patent Application No. 2005/0281790) are silent about that said enriched cell population of mesenchymal precursors are positive for cell markers 3G5 or MUC18/cd146, as recited in claims 71-76, or positive for one or more markers, recited in claim 77, or negative for the markers recited in claim 78, or capable of forming a clonogenic colony, as recited in claims 80 and 81. The Examiner asserted, however, that these limitations would be inherent properties of the referenced cell composition because the referenced cell composition is the same as claimed, and it is applicants' burden to show that the reference cell population does not have the same properties as recited in the claims.

The Examiner also rejected claims 70 and 79 asserting that the claimed functional limitation would allegedly be inherent properties of the referenced enriched cell population and composition comprising said cells. Therefore, according to the Examiner, the reference teachings anticipate the claimed invention.

Applicants' Response

In response, applicants respectfully traverse the Examiner's rejection. However, in order to expedite prosecution, but without conceding the correctness of the Examiner's argument, applicants have hereinabove amended claim 68 to

recite "A population of cells enriched for 3G5 cells, wherein such 3G5 cells are mesenchymal precursor cells which comprise mesenchymal precursor cells capable of giving rise to colony forming unit-fibroblast (CFU-F), and wherein at least 30% of the total cells of the population are positive for the marker 3G5."

Applicants note that neither U.S. Patent No. 7,122,178, nor U.S. Patent Application Publication No. 2005/0281790 teach a population of cells enriched for 3G5 cells, wherein such 3G5 cells are mesenchymal precursor cells which comprise mesenchymal precursor cells capable of giving rise to colony forming unit-fibroblast (CFU-F), and wherein at least 30% of the total cells of the population are positive for the marker 3G5.

The Examiner asserted that U.S. Patent No. 7,122,178 and U.S. Patent Application No. 2005/0281790 teach a population of cells enriched for STRO-1^{bright} MPCs. However, as noted above, enriching for STRO-1^{bright} MPCs does not enrich for MPCs wherein at least 30% of the total cells of the population are positive for the marker 3G5. As the specification of the subject application teaches at page 26, lines 4-16, and Figure 4, with regard to STRO-1^{bright} cells, "bone marrow clonogenic colonies expressed the 3G5 antigen at low levels." In addition, it is stated on page 13, lines 24-26 of the specification that "3G5 positive MPCs constitute about 15% of MPCs based on STRO-1^{bri} colony forming cells."

Accordingly, the claims as modified are not taught explicitly or inherently in U.S. Patent No. 7,122,178 or U.S. Patent Application No. 2005/0281790. Accordingly, U.S. Patent No. 7,122,178 or U.S. Patent Application No. 2005/0281790 do not teach all elements of the claimed invention.

Moreover, the Examiner has acknowledged that the cited patent/application is silent about MUC18/cd146, as recited in claims 71 and 74, or that the population is positive for one or more markers, recited in claim 77, or negative for the markers recited in claim 78, or capable of forming a clonogenic colony, as recited in claims 80 and 81. These limitations would not be inherent properties (to the extent an anticipation rejection based on inherency requires certainty) of the referenced cells composition because the referenced cells are not the same as the claimed invention as explained hereinabove. Therefore, applicants submit that U.S. Patent No. 7,122,178 or U.S. Patent Application No. 2005/0281790 do not anticipate the claimed invention.

Nonstatutory Obviousness-Type Double Patenting Rejection

Rejection Over U.S. Patent No. 7,122,178

The Examiner rejected claims 68-81 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 7,122,178. The Examiner stated that although the conflicting claims are not identical, they allegedly are not patentably distinct from each other because claims 1-13 of U.S. Patent No. 7,122,178 recite an enriched cell population of

mesenchymal precursor cells, enriched for STRO-1^{bright} cells, and capable of giving rise to CFU-F.

Applicants' Response

In response, applicants submit that U.S. Patent No. 7,122,178 claims a population of cells enriched for STRO-1 cells, wherein the enriched cells are mesenchymal precursor cells that are colony forming. The Examiner concedes that none of these documents disclose cell populations enriched for 3G5 expressing MPCs, but asserts that this feature is inherent in the STRO-1 expressing MPCs claimed in U.S. Patent No. 7,122,178.

For reasons discussed above, enriching for STRO-1^{bright} MPCs does not enrich for MPCs wherein at least 30% of the total cells of the population are positive for the marker 3G5.

Therefore, a population of cells enriched for 3G5 cells, wherein such 3G5 cells are mesenchymal precursor cells which comprise mesenchymal precursor cells capable of giving rise to colony forming unit-fibroblast (CFU-F), and wherein at least 30% of the total cells of the population are positive for the marker 3G5 is not obvious from a claim directed to a population of cells enriched for STRO-1^{bright} cells (claim 1 of U.S. Patent No. 7,122,178).

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection Over Co-pending Applications No. 11/169,875 and 10/553,633

The Examiner provisionally rejected claims 68-81 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 52-78 of co-pending Application No. 11/169,875. Although the conflicting claims are not identical, they allegedly are not patentably distinct from each other because claims 52-78 of co-pending Application No. 11/169875 recited an enriched cell population, of mesenchymal precursor cells, enriched for STRO-1^{bright} cells.

The Examiner also provisionally rejected claims 68-81 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 59-65 of co-pending Application No. 10/553,633. Although the conflicting claims are not identical, they allegedly are not patentably distinct from each other because claims 59-65 of co-pending Application No. 10/553,633 recited an isolated human stem cells population, wherein said cells expressed SRTO-1.

Applicants' Response

In response, applicants note that the current rejections are provisional as the cited applications are not patented or allowed. Accordingly, if these provisional rejections are the only outstanding rejections after entry of this amendment and consideration of the arguments presented herein, applicants request that these rejections be withdrawn.

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants directs the Examiner's attention to the following disclosures, which are also listed on the attached substitute Form PTO-1449 (**Exhibit A**). Document 17 is a U.S. Patent, and a copy of this document is not attached hereto as permitted by 37 C.F.R. §1.98(a)(2)(ii). Copies of items 1-16 are enclosed herewith as **Exhibits 1-16** respectively.

1. Yang XB, *et al.* (2006), "Evaluation of Human Bone Marrow Stromal Cell Growth on Biodegradable Polymer/Bioglass Composites," Biochemical And Biophysical Research Communications 342:1098-1107; **(Exhibit 1)**

2. Fujii, S. *et al.* (2008), "Investigating a Clonal Human Periodontal Ligament Progenitor/Stem Cell Line In Vitro and In Vivo," J. Cell. Physiol. 215:743-749; **(Exhibit 2)**

3. Bianco, P. *et al.* (2001), "Bone Marrow Stromal Stem Cells: Nature, Biology, and Potential Applications," Stem Cells 19:180-192;**(Exhibit 3)**

4. Final Office Action issued June 23, 2009 in connection with U.S. Serial No. 11/169,875; **(Exhibit 4)**

5. Final Office Action issued July 16, 2009 in connection with U.S. Serial No. 10/955,709; **(Exhibit 5)**

6. Final Office Action issued Sep 29, 2009 in connection with U.S. Serial No. 10/551,326; **(Exhibit 6)**

7. Final Office Action issued October 08, 2009 in connection with U.S. Serial No. 11/326,736; **(Exhibit 7)**

8. Notice of Allowance issued October 29, 2009 in connection with U.S. Serial No. 10/813,747; **(Exhibit 8)**

9. Final Office Action issued December 9, 2009 in connection with U.S. Serial No. 11/169,875; **(Exhibit 9)**

10. Examination report issued October 10, 2009 in connection with European Application No. 05754008.0; **(Exhibit 10)**

11. Neuhaus T. et al. (2003) "Stromal cell-derived factor 1alpha (SDF-1alpha) induces gene-expression of early growth response-1 (Egr-1) and VEGF in human arterial endothelial cells and enhances VEGF induced cell proliferation" Cell Proliferation. 36:75-86; **(Exhibit 11)**

12. Salcedo R. et al. (1999) "Vascular endothelial growth factor and basic fibroblast growth factor induce expression of CXCR4 on human endothelial cells: In vivo neovascularization induced by stromal-derived factor-1alpha" American Journal of Pathology. 154:1125-1135; **(Exhibit 12)**

13. Office Action issued January 19, 2010 in connection with corresponding Japanese Application No. 2006-503989; **(Exhibit 13)**

14. Office Action issued March, 16 2010 in connection with U.S. Serial No. 11/663,570; **(Exhibit 14)**

15. Kanbe K. et al. (2002) "Stimulation of Matrix Matalloprotease 3 Release from Human Chondrocytes by the Interaction of Stromal Cell-Derived Factor 1 and CXC Chemokine Receptor 4" Arthritis & Rheumatism 46:130-137; **(Exhibit 15)**

16. Final Office Action issued June 2, 2010 in connection with U.S. Serial No. 11/169,875p; **(Exhibit 16)**

17. U.S. Patent No. 5,580,754 issued to Samal on December 3, 1996.

The Examiner is respectfully requested to make of record each item listed on Form PTO-1449 Substitute by initialing and dating the attached Form PTO-1449 Substitute, and returning a copy of the initialed and dated form to applicants' undersigned attorney.

This Supplemental Information Disclosure Statement is being submitted under 37 C.F.R. §1.97(b)(4), after the filing of a request for continued examination under 37 C.F.R. §1.113. Accordingly, no fee is required for filing this Supplemental Information Disclosure Statement.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed total fee of $1,580.00, including $405.00 for filing a Request for Continued Examination and $1,175.00 for a five-month extension of time, is deemed necessary in connection with the filing of this Amendment and Supplemental Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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